

In the claims:

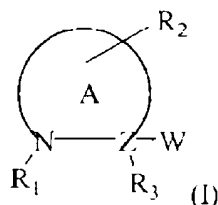
For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

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1. (Amended) A method for modifying, in an animal, metabolism of glucagon-like peptide 1 (GLP-1), comprising administering to the animal a composition including one or more inhibitors of a dipeptidylpeptidase which inactivates GLP-1, which inhibitor(s) inhibit(s) the dipeptidylpeptidase proteolysis of GLP-1 at a K_i of 1 nM or less.

 2. A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis having a K_i of 1 nM or less.

 3. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1) having a K_i of 1 nM or less.
 4. (Amended) A method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) which have a K_i of 1 nM or less.
 5. (Amended) The method of claim 1, wherein the dipeptidylpeptidase is DPIV.
 6. (Amended) The method of claim 2 or 3, wherein the protease inhibitor is an inhibitor of DPIV.
 7. (Amended) The method of claim 2 or 3, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

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8. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.
 9. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.
 10. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for immunosuppression in the μM or greater range.
 11. (Amended) The method of any of claim 1, 2, 3 or 4, wherein the inhibitor has a K_i for DPIV inhibition of 0.5 nM or less.
 12. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is peptidomimetic of a peptide selected from the group consisting Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.
 13. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has a molecular weight less than 7500 amu.
 14. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is administered orally.
 15. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is represented by the general Formula I;

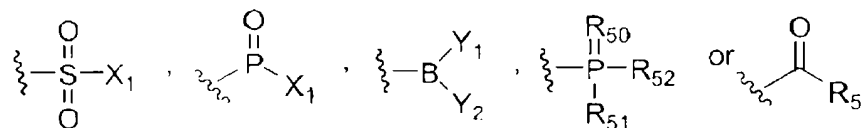


wherein,

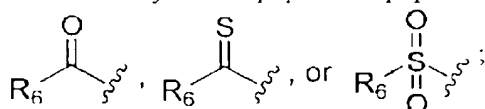
A represents a 4-8 membered heterocycle including a N and a C α carbon;

Z represents C or N;

W represents -CN, -CH=NR₅,



R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



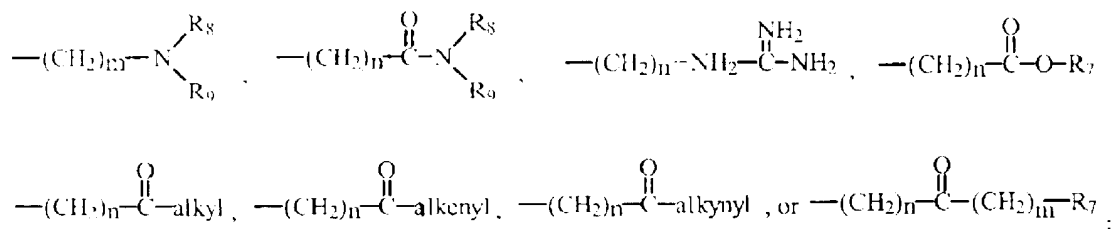
R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

if Z is N, then R₃ represents a hydrogen;

if Z is C, then R₃ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_m-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, (CH₂)_n-S-alkyl, (CH₂)_n-S-alkenyl, (CH₂)_n-S-alkynyl, (CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR₇;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



B.S.
 R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(\text{CH}_2)_m-\text{R}_7$, $-\text{C}(=\text{O})-\text{alkyl}$, $-\text{C}(=\text{O})-\text{alkenyl}$, $-\text{C}(=\text{O})-\text{alkynyl}$, or $-\text{C}(=\text{O})-(\text{CH}_2)_m-\text{R}_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3 , SH, NH_2 , NO_2 or OR'_7 ;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7 , or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a hydrogen or a halogen, or a hydroxyl;

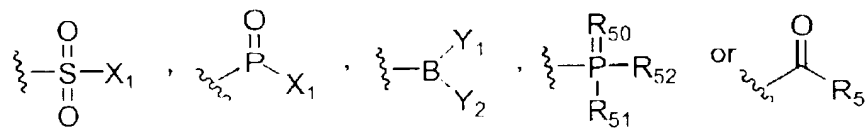
X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

16. (Amended) The method of claim 15, wherein,

W represents $-\text{CN}$, $-\text{CH}=\text{NR}_5$,



R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_m-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkenyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;

R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

Y₁ and Y₂ can independently or together be hydroxyl, , an alkoxy, or, taken together, Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure which can be hydrolyzed to hydroxy groups;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

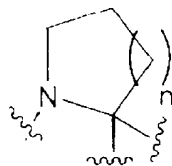
X₁ represents a hydrogen or a halogen, or a hydroxyl;

X₂ and X₃ each independently represent a hydrogen or a halogen.

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

17. (Amended) The method of claim 15, wherein the ring A is represented by the formula

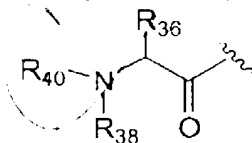


wherein,

n is an integer of 1 or 2.

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18. (Amended) The method of claim 15, wherein W represents ---B--- $\begin{matrix} Y_1 \\ Y_2 \end{matrix}$ or ---C(=O)---R_5 .

19. (Amended) The method of claim 15, wherein R₁ represents

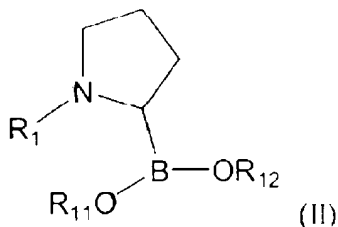


R₃₆ represents a small hydrophobic group and R₃₈ is hydrogen, or, R₃₆ and R₃₈ together form a 4-7 membered heterocycle including the N and the C α carbon, as defined for A above; and

R₄₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

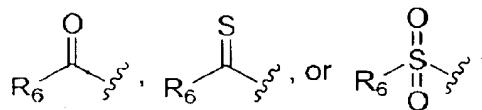
20. (Amended) The method of claim 15, wherein R₂ is absent, or represents a small hydrophobic group.
21. (Amended) The method of claim 15, wherein R₃ is a hydrogen, or a small hydrophobic group.
22. (Amended) The method of claim 15, wherein R₅ is a hydrogen, or a halogenated lower alkyl.
23. (Amended) The method of claim 15, wherein X₁ is a fluorine, and X₂ and X₃, if halogens, are fluorine.

24. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formula (II):

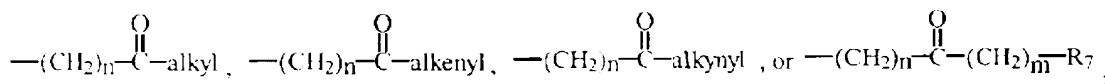
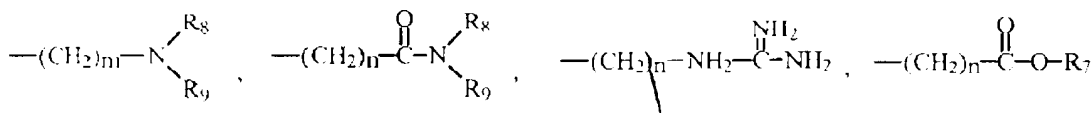


wherein,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or



R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, - (CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-(CH₂)_m-R₇,

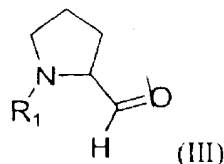
or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₁₁ and R₁₂ each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or R₁₁ and R₁₂ taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and

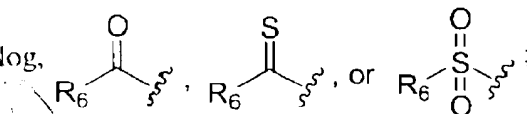
n is an integer in the range of 1 to 8.

25. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formula III,

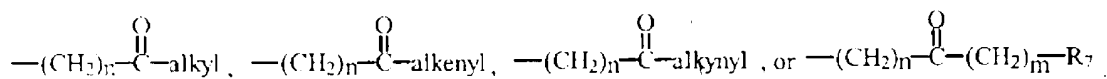
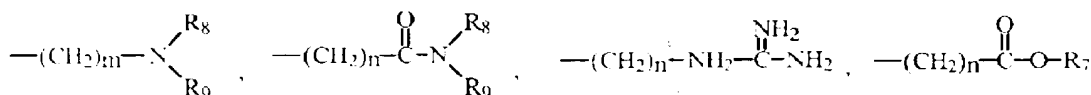


wherein,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,



R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

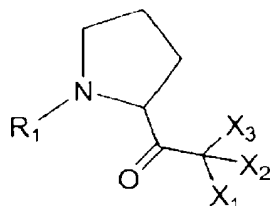
R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(-O)-alkyl, -C(-O)-alkenyl, -C(-O)-alkynyl, or -C(-O)-(CH₂)_m-R₇.

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure:

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

26. (Amended) The method of claim 15, wherein the inhibitor is represented by the general formula:

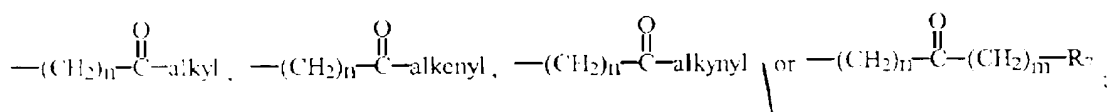
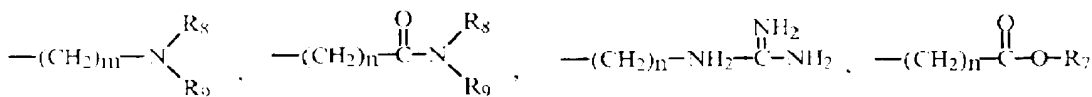


wherein,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-

terminally linked peptide or peptide analog, $R_6-\overset{\text{O}}{\parallel}{C}-$, $R_6-\overset{\text{S}}{\parallel}{C}-$, or $R_6-\overset{\text{O}}{\parallel}{S}(=O)-$;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)$ -alkyl, $C(=O)$ -alkenyl, $-C(=O)$ -alkynyl, $-C(=O)-(CH_2)_m-R_7$,

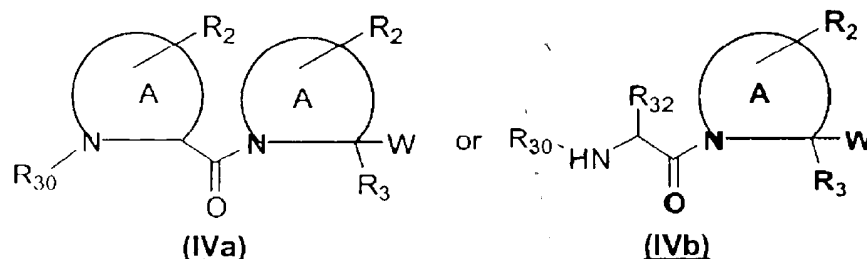
or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

X_1 , X_2 and X_3 each represent a hydrogen or a halogen; and

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

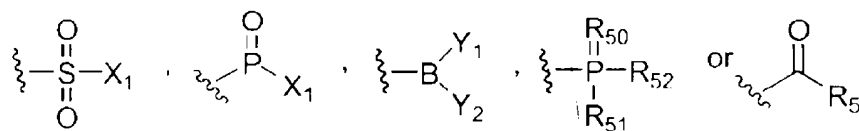
27. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formulae IVa or IVb:



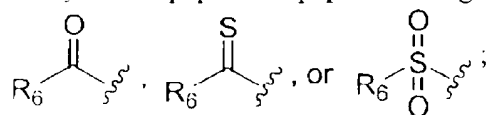
wherein,

A represent a 4-8 membered heterocycle including a N and a C α carbon;

W represents $-CN$, $-CH-NR_5$,



R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,

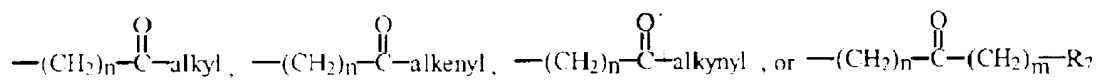
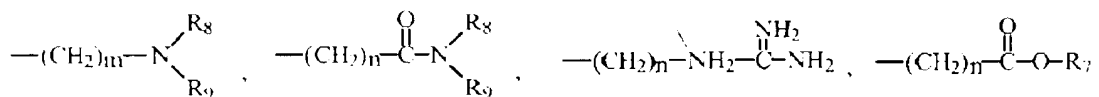


R_3 represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, -

$(\text{CH}_2)_m\text{-O-lower alkyl}$, $-(\text{CH}_2)_m\text{-O-lower alkenyl}$, $-(\text{CH}_2)_n\text{-O}-(\text{CH}_2)_m\text{R}_7$, $-(\text{CH}_2)_m\text{-SH}$, $-(\text{CH}_2)_m\text{-S-lower alkyl}$, $-(\text{CH}_2)_m\text{-S-lower alkenyl}$, or $-(\text{CH}_2)_n\text{-S}-(\text{CH}_2)_m\text{-R}_7$;

R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-\text{C}(\text{X}_1)(\text{X}_2)\text{X}_3$, $-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-OH}$, $-(\text{CH}_2)_n\text{-O-alkyl}$, $-(\text{CH}_2)_n\text{-O-alkenyl}$, $-(\text{CH}_2)_n\text{-O-alkynyl}$, $-(\text{CH}_2)_n\text{-O}-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-SH}$, $-(\text{CH}_2)_n\text{-S-alkyl}$, $-(\text{CH}_2)_n\text{-S-alkenyl}$, $-(\text{CH}_2)_n\text{-S-alkynyl}$, $-(\text{CH}_2)_n\text{-S}-(\text{CH}_2)_m\text{-R}_7$, $-\text{C}(\text{O})\text{C}(\text{O})\text{NH}_2$, or $-\text{C}(\text{O})\text{C}(\text{O})\text{OR}'_7$;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_m\text{-OH}$, $-(\text{CH}_2)_m\text{-O-alkyl}$, $-(\text{CH}_2)_m\text{-O-alkenyl}$, $-(\text{CH}_2)_m\text{-O-alkynyl}$, $-(\text{CH}_2)_m\text{-O}-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_m\text{-SH}$, $-(\text{CH}_2)_m\text{-S-alkyl}$, $-(\text{CH}_2)_m\text{-S-alkenyl}$, $-(\text{CH}_2)_m\text{-S-alkynyl}$, $-(\text{CH}_2)_m\text{-S}-(\text{CH}_2)_m\text{-R}_7$,



R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(\text{CH}_2)_m\text{-R}_7$, $\text{C}(=\text{O})\text{-alkyl}$, $\text{C}(=\text{O})\text{-alkenyl}$, $\text{C}(=\text{O})\text{-alkynyl}$, or $\text{C}(=\text{O})\text{-(CH}_2)_m\text{-R}_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{32} is a small hydrophobic group;

R_{30} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group;

R_{50} represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR⁺₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR⁺₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

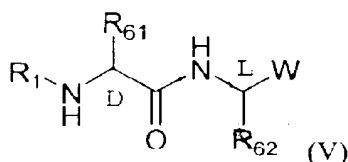
X₁ represents a hydrogen or a halogen, or a hydroxyl;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

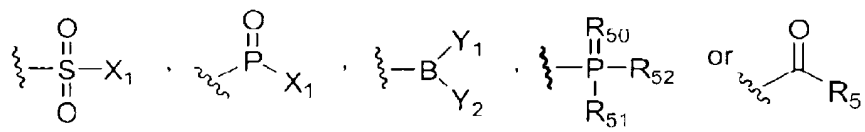
n is an integer in the range of 1 to 8.

28. 28. (Amended) The method of claim 1, 2, 3, 4, or 15, wherein the inhibitor is represented by the general Formula V:

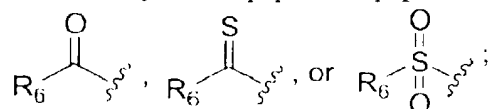


wherein,

W represents a functional group which reacts with an active site residue of the targeted protease, selected from -CN, -CH=NR₅,



R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a

nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R_5 represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$ -alkyl, $-(CH_2)_n-O$ -alkenyl, $-(CH_2)_n-O$ -alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$ -alkyl, $-(CH_2)_n-S$ -alkenyl, $-(CH_2)_n-S$ -alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

BS cont.
 R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -alkyl, $-(CH_2)_m-O$ -alkenyl, $-(CH_2)_m-O$ -alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -alkyl, $-(CH_2)_m-S$ -alkenyl, $-(CH_2)_m-S$ -alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_{61} and R_{62} , independently, represent small hydrophobic groups;

Y_1 and Y_2 can independently or together be OH or an alkoxyl, or, taken together, Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

R_{50} represents O or S;

R_{51} represents N_3 , SH, NH_2 , NO_2 or OR'_7 ;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7 , or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

X_2 and X_3 , independently for each occurrence, represent a hydrogen or a halogen;

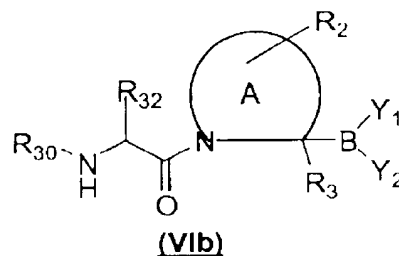
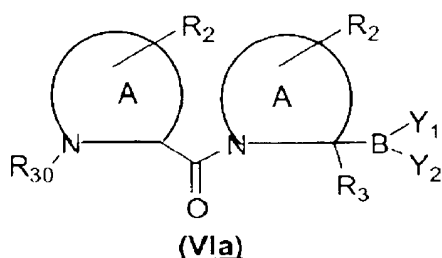
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

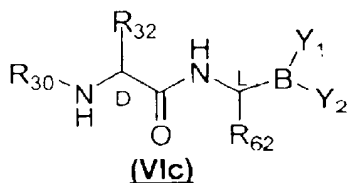
29. (Amended) A method for modifying, in an animal, metabolism of peptide hormone, comprising administering to the animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) with K_i s of 1 nM or less, which peptide hormone is selected from glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

30. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

31. (Amended) The method of claim 30, wherein the boronyl peptidomimetic is represented in the general Formulae VIa c,



or



wherein,

each A independently represents a 4-8 membered heterocycle including an N and a C α carbon;

R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

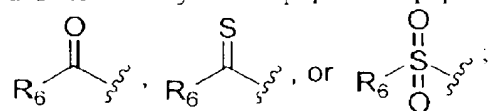
R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -alkyl, $-(CH_2)_m-O$ -alkenyl, $-(CH_2)_m-O$ -alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -alkyl, $-(CH_2)_m-S$ -alkenyl, $-(CH_2)_m-S$ -alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

R₃₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



R₃₂ represents lower alkyl or halogen;

Y_1 and Y_2 can independently or together be OH or an alkoxy, or, taken together, Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

R_{62} represents lower alkyl or halogen;

m is zero or an integer in the range of 1 to 8; and

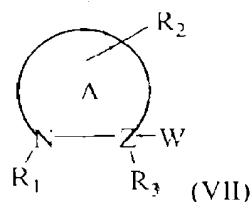
n is an integer in the range of 1 to 8.

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cadd.
32. (Amended) The method of claim 31, wherein administering the boronyl peptidomimetic reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.
 33. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.
 34. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.
 35. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for immunosuppression in the μ M or greater range.
 36. (Amended) The method of claim 31, wherein the boronyl peptidomimetic is administered orally.
 37. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition comprising a peptidomimetic boronyl inhibitor wherein the peptide to be mimicked is selected from Pro-Pro, Ala-Pro, and (D) Ala-(L)-Ala.

Please add the following new claims:

38. (New) A method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis.
39. (New) A method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1).
40. (New) A method for modifying, in a glucose intolerant animal, metabolism of a peptide hormone, comprising administering to the animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) with in an amount sufficient to increase the plasma half-life of the peptide hormone, which peptide hormone is selected from glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.
41. (New) A method for modifying glucose metabolism of a glucose intolerant animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.
42. (New) The method of any of the claims 38-41 wherein, the glucose intolerance in the animal is a result of a deletion or disruption of the gene encoding for a glucagon type peptide.
43. (New) The method of claim 42 wherein, the glucagon type peptide is GLP-1 or GLP-2.
44. (New) The method of claim 38, wherein the dipeptidylpeptidase is DPIV.
45. (New) The method of claim 38 or 39, wherein the protease inhibitor is an inhibitor of DPIV.

46. (New) The method of claim 38 or 39, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.
47. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.
48. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range
49. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an EC_{50} for immunosuppression in the μM or greater range.
50. (New) The method of any of claim 38, 39, 40, or 41, wherein the inhibitor has a K_i for DPIV inhibition of 0.5 nM or less.
51. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.
52. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has a molecular weight less than 7500 amu.
53. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is administered orally.
54. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is represented by the general Formula VII;

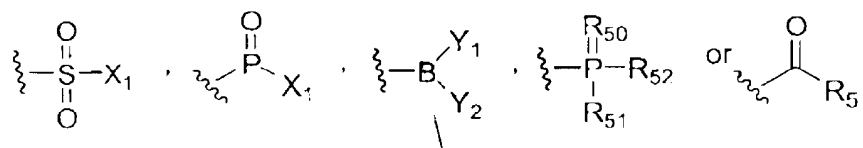


wherein,

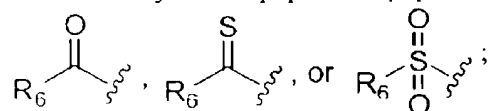
A represents a 4-8 membered heterocycle including a N and a C α carbon;

Z represents C or N;

W represents -CN, -CH=NR₅,



R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,



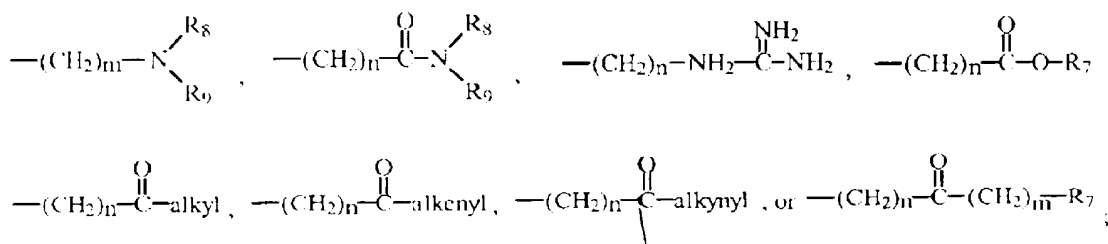
R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

if Z is N, R₃ represents a hydrogen;

if Z is C, R₃ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_n-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkenyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-(CH₂)_m-R₇,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a hydrogen or a halogen, or a hydroxyl;

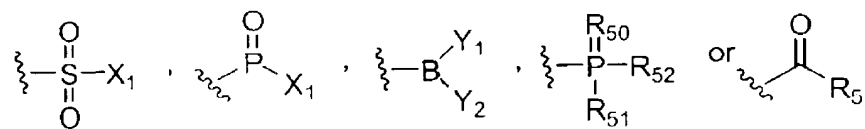
X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

55. (New) The method of claim 54, wherein,

W represents $-\text{CN}$, $-\text{CH}=\text{NR}_5$,



R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-\text{C}(\text{X}_1)(\text{X}_2)\text{X}_3$, $-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-OH}$, $-(\text{CH}_2)_n\text{-O-alkyl}$, $-(\text{CH}_2)_n\text{-O-alkenyl}$, $-(\text{CH}_2)_n\text{-O-alkynyl}$, $-(\text{CH}_2)_n\text{-O}-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-SH}$, $-(\text{CH}_2)_n\text{-S-alkyl}$, $-(\text{CH}_2)_n\text{-S-alkenyl}$, $-(\text{CH}_2)_n\text{-S-alkynyl}$, $-(\text{CH}_2)_n\text{-S}-(\text{CH}_2)_m\text{-R}_7$, $-\text{C}(\text{O})\text{C}(\text{O})\text{NH}_2$, or $-\text{C}(\text{O})\text{C}(\text{O})\text{OR}'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

Y_1 and Y_2 can independently or together be hydroxyl, or taken together Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

R_{50} represents O or S;

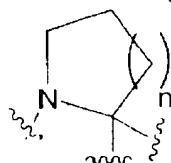
R_{51} represents N_3 , SH, NH_2 , NO_2 or OR'_7 ;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7 , or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a hydrogen or a halogen, or a hydroxyl; and

X_2 and X_3 each represent a hydrogen or a halogen.

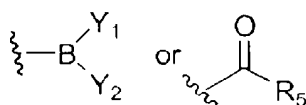
56. (New) The method of claim 54, wherein the ring A is represented by the formula



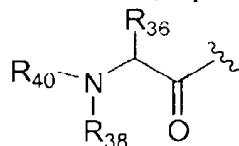
wherein,

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 n is an integer of 1 or 2.

57. (New) The method of claim 54, wherein W represents



58. (New) The method of claim 54, wherein R_1 represents

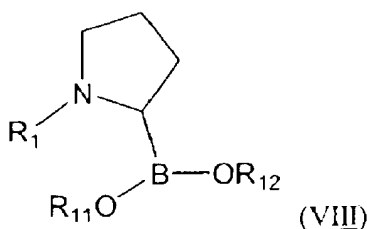


R_{36} represents a small hydrophobic group and R_{38} is hydrogen, or, R_{36} and R_{38} together form a 4-7 membered heterocycle including the N and the $C\alpha$ carbon, as defined for A above; and

R_{40} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

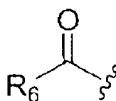
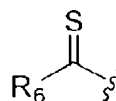
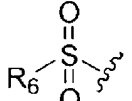
59. (New) The method of claim 54, wherein R_2 is absent, or represents a small hydrophobic group.

60. (New) The method of claim 54, wherein R_3 is a hydrogen, or a small hydrophobic group.
61. (New) The method of claim 54, wherein R_5 is a hydrogen, or a halogenated lower alkyl.
62. (New) The method of claim 54, wherein X_1 is a fluorine, and X_2 and X_3 , if halogens, are fluorine.
63. (New) The method of claim 54, wherein the inhibitor is represented by the general Formula (VIII):

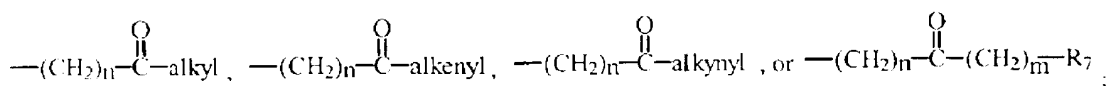
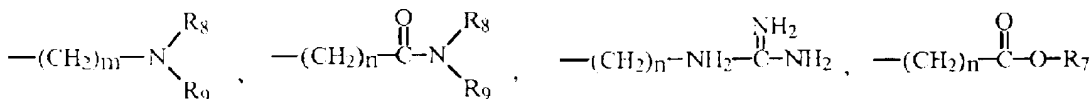


wherein,

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-

terminally linked peptide or peptide analog, R_6 , R_6 , or R_6 ;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, $-(CH_2)_m-S-(CH_2)_m-R_7$,



R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

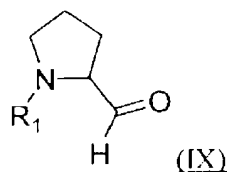
R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)-alkyl$, $-C(=O)-alkenyl$, $-C(=O)-alkynyl$, or $-C(=O)-(CH_2)_m-R_7$, or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{11} and R_{12} each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or R_{11} and R_{12} taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and

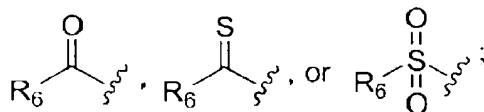
n is an integer in the range of 1 to 8.

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64. (New) The method of claim 54, wherein the inhibitor is represented by the general Formula IX,

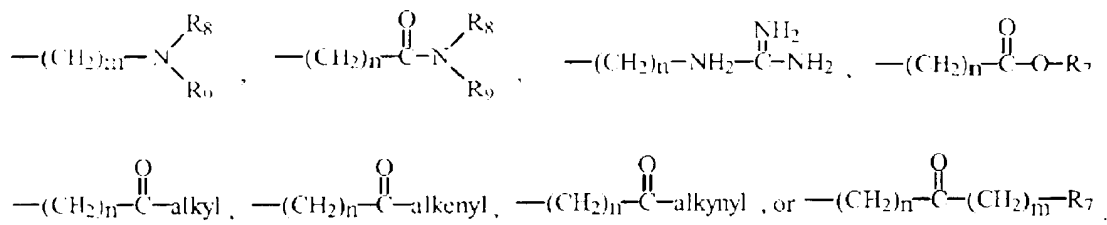


wherein

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,



R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, $-(CH_2)_m-S-(CH_2)_m-R_7$,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

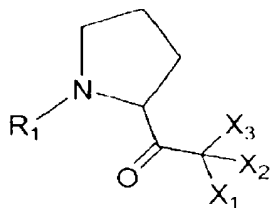
R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, $-(\text{CH}_2)_m-\text{R}_7$, $-\text{C}(-\text{O})-\text{alkyl}$, $-\text{C}(=\text{O})-\text{alkenyl}$, $-\text{C}(=\text{O})-\text{alkynyl}$, or $-\text{C}(=\text{O})-(\text{CH}_2)_m-\text{R}_7$,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and

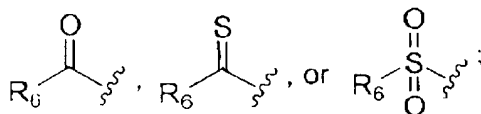
n is an integer in the range of 1 to 8.

65. (New) The method of claim 54, wherein the inhibitor is represented by the general formula:



wherein,

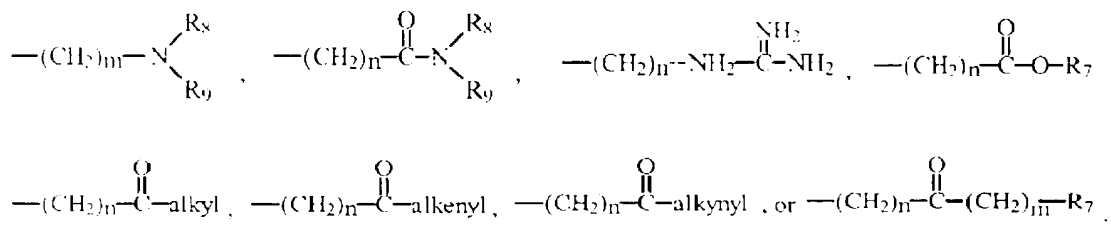
R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,



R₄ represents a small hydrophobic group;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(\text{CH}_2)_m-\text{R}_7$, $-(\text{CH}_2)_m-\text{OH}$, $-(\text{CH}_2)_m-\text{O}-\text{alkyl}$, $-(\text{CH}_2)_m-\text{O}-\text{alkenyl}$, $-(\text{CH}_2)_m-\text{O}-$

alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -alkyl, $-(CH_2)_m-S$ -alkenyl, $-(CH_2)_m-S$ -alkynyl, $-(CH_2)_m-S-(CH_2)_m-R_7$,



R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(-O)-alkyl$, $-C(=O)-alkenyl$, $-C(=O)-alkynyl$, $-C(=O)-(CH_2)_m-R_7$.

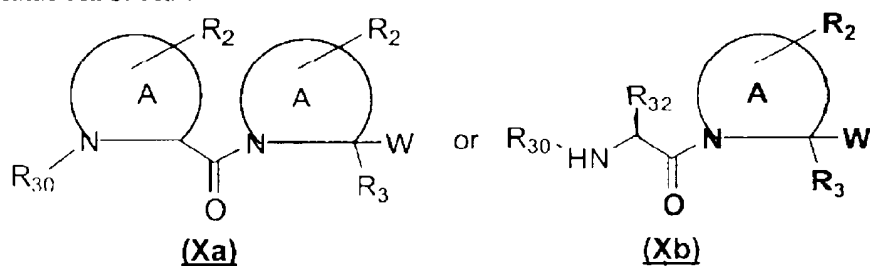
or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

X_1 , X_2 and X_3 each represent a hydrogen or a halogen; and

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

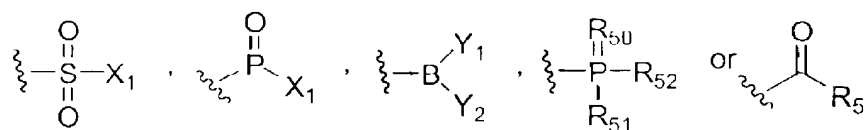
66. (New) The method of claim 54, wherein the inhibitor is represented by the general Formulae Xa or Xb :



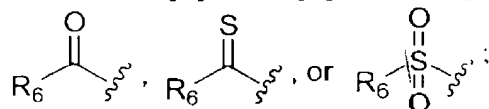
wherein,

A represents a 4-8 membered heterocycle including a N and a C α carbon;

W represents -CN, -CH=NR₅.



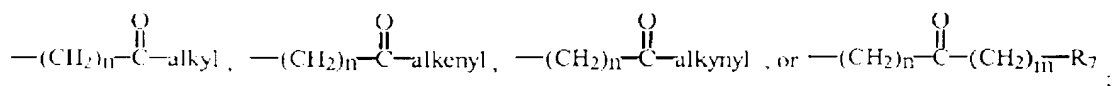
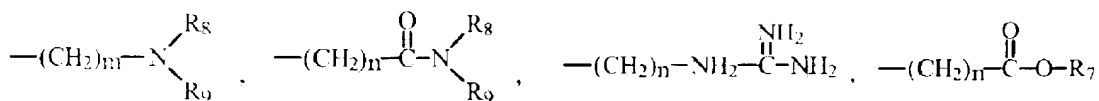
R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,



R₃ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_n-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkenyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(-O)-alkenyl, -C(=O)-alkynyl, or -C(-O)-(CH₂)_m-R₇, or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₃₂ is a small hydrophobic group;

R₃₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

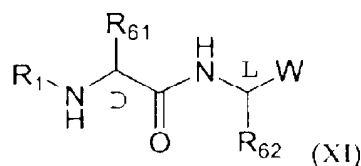
X₁ represents a hydrogen or a halogen, or a hydroxyl;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

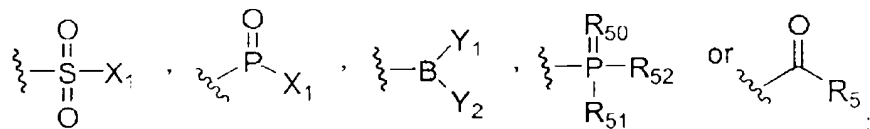
n is an integer in the range of 1 to 8.

67. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is represented by the general Formula XI:

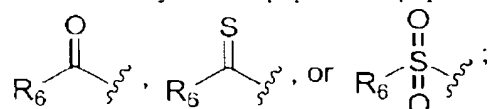


wherein.

W represents a functional group which reacts with an active site residue of the targeted protease selected from -CN, -CH=NR₅,



R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents H, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_m-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkenyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;

R₆ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, or -(CH₂)_m-S-(CH₂)_m-R₇;

R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R₆₁ and R₆₂, independently, represent small hydrophobic groups;